UNITED STATES DISTRICT COURT
WESTERN DISTRICT OF WISCONSIN

PROMEGA CORPORATION,

Plaintiff,

MAX-PLANCK-GESELLSCHAFT ZUR FORDERUNG DER WISSENSCHAFTEN E.V.,

Involuntary Plaintiff,

v.

LIFE TECHNOLOGIES CORPORATION, INVITROGEN IP HOLDINGS, INC., and APPLIED BIOSYSTEMS, INC.,

Defendants.

Case No.: 10-CV-281

DECLARATION OF RANDALL L. DIMOND, PH.D. IN SUPPORT OF PROMEGA CORPORATION'S OPENING CLAIMS CONSTRUCTION BRIEF

I, Randall L. Dimond, declare pursuant to 28 U.S.C. § 1746 as follows:

1. I am the Vice-President and Chief Technical Officer of Promega Corporation ("Promega") and previously provided a number of declarations in this case.

2. The named inventors of the Promega Patents, i.e. U.S. Patent Nos. 5,843,660 ('660); 6,221,598 ('598); 6,479,235 ('235); and 7,008,771 ('771), are familiar to me. Some of them reported directly to me at various periods in time and I had responsibility for overseeing their work during the time periods of these inventions. I am familiar with the technology utilized in these patents as well as the Tautz Patent (U.S. Patent No. RE37,984).

3. I supply this Declaration in support of Plaintiff's Opening Claim Construction Brief. In particular, I have attempted to assist the court in understanding the technology.

4. The human genome is comprised of the DNA present in the 23 pairs of chromosomes existing in the nucleus of human cells. This genomic DNA is made of two complementary "strands" or "sequences" of "nucleotides" or "bases." The nucleotides in DNA are only four in number and are paired in a defined manner. The four nucleotides are adenine (A), thymine (T), guanine (G) and cytosine (C). An (A) is complementary to, and pairs only with (T); a (C) is complementary to, and pairs only with a (G).

5. The combinations of genetic information at multiple locations in genomic DNA are unique to each individual. It is this fact that forms the premise for genetic identity testing. To use DNA to identify an individual, one can target and identify certain locations or "loci" on the chromosomes which are polymorphic within a population, i.e., loci that vary from individual to individual within the population. These loci are useful as identifiers only when they exhibit a high degree of variation within the population, since if they were largely the same from individual to individual within the population, their ability to distinguish any one individual from another would be minimal.

6. The more a specified locus varies within a population, i.e., the more it varies from individual to individual, the more "polymorphic" the locus is said to be. No one locus alone, however, will positively identify an individual to a

statistically significant degree, since no one locus is unique to each individual within any given population. Consequently, for purposes of forensic and paternity determinations, the identification of multiple polymorphic loci is necessary. Indeed, the more polymorphic the loci used in the identification process, the more accurate the identification becomes because the statistical probability of a match between the DNA sample and the individual in question increases exponentially as additional matching loci are identified.

7. The goal is to use enough loci with sufficient polymorphic characteristics such that the identification is so statistically significant that the result cannot be reasonably disputed, i.e., the individual is identified beyond any reasonable doubt. For example, using Promega's genetic identity products, one can identify an individual's DNA with a power of discrimination exceeding 1 in 100,000,000,000.

8. STRs are loci found within genomic DNA that have a number of short repetitive nucleotide sequences. Different authors have slightly different definitions with regard to the repeat length that is considered an STR. Any differences in these definitions, however, do not appear to have impact on any issues in this case.

9. The DNA sequences at a particular STR locus within a given population will exhibit a variable number of these repeat sequences. For some individuals within a given population the sequence will repeat 7 times, for others 8 times, for others 4 and so on. It is this variation in the number of repeats at a

particular locus that is responsible for the polymorphism, which permits scientists to genetically distinguish one individual from another.

10. The particular genetic information or base sequence associated with a segment of DNA at a particular STR locus in one individual, is called an "allele." The alleles are numbered in accordance with the number of repeated nucleotide motifs (the "motif" is the specific nucleotide sequence, e.g., AATG, of the short tandem repeat).

11. To understand the meaning of the term "co-amplifying" in step (c) of these various independent method Claims of the Promega Patents, it is helpful to understand the commonly known term "amplifying." The term "amplify" refers to a process in which multiple copies of the alleles present at the STR loci are made. The STR regions of the DNA must be "amplified" to be visualized or detected because they are present in too low a concentration to be detected among the rest of the human DNA.

12. PCR is one method of amplifying. There are several steps in the PCR process. First, the "double stranded" or two strands of genomic DNA are separated or "denatured," thereby forming "single stranded" DNA. This denaturation step is done by heating the DNA to a certain temperature, which is sufficient to cause the two strands to separate. Second, a pair of PCR "primers" is introduced and allowed to hybridize or pair with the single stranded DNA. "Hybridization" occurs when the PCR primers "anneal" or join to a single strand of the DNA. This hybridization occurs in accordance with the nucleotide pairing rules (e.g. A with T, etc.) noted above, i.e., at a point on the

single stranded DNA where the PCR primer sequence is complementary to the genomic nucleotide sequence. Referring to the two opposing primers as the "forward" or "reverse" PCR primer differentiates each primer in the pair.

13. There is a definition of "primers" or "primer" in the specifications of all of the Promega Patents and these definitions are consistent with how the term is understood to one skilled in the art.

14. The PCR primers hybridize at points on the genomic DNA that are adjacent to, or "flank," the actual STR locus. These "flanking regions" are used as the point of hybridization because they are not polymorphic, i.e., they contain the same sequence of nucleotides for all individuals within a given population even though the number of repeats contained in the STR locus between the flanking regions varies from individual to individual. This ensures that all alleles in all individuals will be amplified.

15. The third step of the PCR process is extension of the primers that have hybridized to the single stranded DNA molecules to convert them into double stranded molecules. An enzyme known as a "DNA polymerase" accomplishes this extension process. The polymerase reads the sequence of the single stranded DNA beginning at the primer location and attaches the complementary nucleotides to the primer guided by the opposite strand (As to Ts and Cs to Gs), thereby making it double stranded. These three steps are then repeated many times to amplify the locus of interest.

16. Amplifying the alleles present at a single STR locus is commonly referred to as a "monoplex" reaction. If one wanted to use eight STR loci in an analysis

of a particular sample, one could carry out eight separate monoplex reactions amplifying eight separate STR loci. Monoplexing was the initial method employed when using STR loci for DNA analysis.

17. Multiplexing is key to realizing the advantages of STRs for determining genetic identity. Often, one must be able to analyze multiple STRs from a relatively small amount of sample. That could only be accomplished if it were possible to multiplex the amplification of STR alleles in such a way that you could still determine all of the alleles present at each locus. The Promega Patents accomplished that result.

18. In order to determine the amplified alleles that are present, they are typically segregated from the amplification (e.g. PCR) reaction mixture or otherwise individually detected. One such process used to separate the alleles is known as "electrophoresis." Polyacrylamide gel electrophoresis (PAGE) is one type of electrophoresis that can be used. Capillary gel electrophoresis (CE) is another type of electrophoresis that can be used.

19. While the term "gel" is used in the various patents of this case, the nature of the gel need not be (and typically is not) the same for each technique. Agarose gels used to separate DNA are not crosslinked and typically comprise between 1 and 3% agarose, which is a linear polymer made up of disaccharide (sugar) units. Polyacrylamide gels used in slab gels (discussed more below) are typically crosslinked. Uncrosslinked polyacrylamide is frequently used in CE, although it may or may not be called a "gel" because it may not be semi-solid.

20. The polyacrylamide gel electrophoresis (or "PAGE") process typically involves the preparation of a polyacrylamide gel between two glass plates, where the gel polymerizes to form a so-called "slab gel." The amplified alleles are then applied to a "well" at the top of the gel, and an electric current is applied to the gel. The amplified alleles will move down the lane below the well, with smaller DNA amplification products (i.e., lower molecular weight products) that contain the amplified STR alleles moving down the gel faster than the larger amplification products (i.e. higher molecular weight products). The various different sizes of the amplification products are separated in this fashion and appear as "bands" on the gel.

21. The alleles from one DNA sample can then be compared to the alleles of a second DNA sample by, for example, running the two samples side-by-side on the gel. One can then determine whether or not the two samples came from the same individual. Additionally a "size marker" or "allelic ladder" is often run concurrently with the sample either mixed with the sample or in another lane of the gel. By comparing the alleles amplified in the DNA sample to the allelic ladder one can determine precisely which alleles appear in the DNA sample.

22. Like the PAGE technique, separation of the PCR products using capillary gel electrophoresis or CE is based primarily on size. There is nothing in the specifications of the Promega Patents to suggest that the "capillary gel" must be cross-linked. POP-4, which is employed in the examples of the '235 Patent

comprises so-called "entangled poly(N,N-dimethylacrylamide)" (or PDMA) which is not cross-linked.

23. The '984 Tautz Patent primarily uses the term "gel" in its unmodified general sense throughout the specification and in the claims. For example Claim 25 is limited only to "a suitable electrophoretic gel," which would be understood by one skilled in the art to include both non-cross-linked (e.g. agarose) and cross-linked gels.

I declare under penalty of perjury that the foregoing is true and correct.

30 March 2011
Dated

Dr. Randall L. Dimond